LESSON OF THE MONTH

Intestinal perforation in a patient with severe ankylosing spondylitis

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Case history

A 54 year old man who had suffered from predominantly axial ankylosing spondylitis for 25 years was referred to see a gastroenterologist because of pallor in 1983. He was found to be anaemic, haemoglobin (Hb) 7.7 g/dl (13–18), mean cell volume (MCV) 57 fl (78–98), mean corpuscular haemoglobin (MCV) 17.5 pg (27.5–32.5), ferritin 27 μg/l (41–480), B12 and folate within normal limits, and to have a raised plasma viscosity 2.17 cps (1.5–1.72). He was taking indomethacin 25 mg thrice daily. Upper gastrointestinal endoscopy and barium enema were normal. The small bowel was not visualised and despite a microcytic hypochromic picture an anaemia of chronic disease was diagnosed. The haemoglobin had subsequently returned towards normal limits, Hb 10.3 g/dl, MCV 66 fl, MCH 20.3 pg, and ferritin 58 μg/l, when reviewed one year later.

At the age of 60 years the patient attended the rheumatology department for the first time. Severe, predominantly axial, ankylosing spondylitis was noted with no lumbar spine movement and only 1 cm of chest expansion. Ranitidine 150 mg twice daily was added to the indomethacin for empirical gastrointestinal protection.

At the age of 63 years the patient underwent a C2-C6 laminectomy for severe upper limb parasthesia. Later that year he was admitted as a general medical patient with suspected melaena with Hb 10.6 g/dl, MCV 75 fl (folate, B12, iron, and total iron binding capacity values were not recorded). A barium swallow was normal. Misoprostol was started in place of the ranitidine. The patient was advised to discontinue the indomethacin. However, because of good symptomatic relief this advice was not taken.

One year later, at the age of 64 years the patient was again admitted to a general medical ward with suspected melaena, Hb 10.2 g/dl, MCV 66.7 fl. Upper gastrointestinal endoscopy was normal. It was assumed that the suspected melaena was secondary to non-steroidal anti-inflammatory drug (NSAID) use despite normal endoscopy, and that the anaemia was also a consequence of the chronic severe disease. A left total hip replacement was also carried out that year.

The following year, at the age of 65 years the patient had lumbar decompressive surgery for leg pain and parasthesia. Later that year significant respiratory difficulties developed and it was noted that the patient had developed narrowing at the vocal cords as a consequence of increasing cervical kyphosis. Indeed the patient was breathing through only a 3 mm laryngeal aperture. This was improved to 3.5 mm with surgery, entailing external laryngeal aryetnoidectomy and lateralisation of the cords.

One year later, at the age of 66 years he was admitted under the ENT surgeons for stridor at rest. This was treated successfully with humidified oxygen and prednisolone. On this occasion the patient was again anaemic with Hb 7.7 g/dl, MCV 70.5 fl, and MCH 22.6 pg. The patient was advised to discontinue the indomethacin and several units of blood were transfused but no additional investigations were performed. It was again assumed that the anaemia reflected NSAID associated blood loss together with anaemia of chronic disease.

One month after discharge from this admission the patient again represented to the general physicians complaining of abdominal pain. No clear cause for the pain was initially identified although gastritis was suspected. Despite advice to the contrary the patient continued the indomethacin. The abdominal pain reached a peak on the fourth day of admission and the patient stopped his indomethacin. Later however the abdominal pain worsened and his condition deteriorated, examination showed a rigid abdomen and an erect chest *x* ray showed free air under the diaphragm. After fibreoptic intubation lasting 45 minutes the patient had a laparotomy. This showed a perforated section of small bowel with numerous gangrenous areas and multiple perforations and an ileal stricture of 11 cm. Histological examination confirmed Crohn's disease. The patient died in the intensive care unit three days later from overwhelming sepsis.

Discussion

This case clearly shows the association between Crohn's disease and ankylosing spondylitis. The patient had several reported episodes of anaemia but only on one occasion in 1984, at the start of the recorded episodes of

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Table 1 Characteristics of the anaemia of chronic disorders compared with normal and iron deficiency anaemia

	Normal	*Iron deficiency anaemia*	*Anaemia of chronic disorders*
Morphology of blood	Normochromic normocytic	Hypochromic microcytic	Normo or hypochromic normocytic: rarely microcytic
Plasma iron (μmol/l)	20.6 +/- 9	Low < 7.2	Low < 12
TIBC (μmol/l)	58.0 +/- 5	High 71.6 +/- 9	Low 44.8 +/- 9
Serum ferritin (μg/l)	100 +/- 60	Low < 10	Often high > 200
Reticuloendothelial iron	Present	Absent	Increased

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anaemia, was the lower bowel investigated, and at no point was the small bowel investigated. The patient was a difficult man and frequently refused advice. For many years before his death the severity of his ankylosing spondylitis, as evidenced by cervical and lumbar surgery, bilateral hip replacements, and major ENT surgery, made investigations more difficult. The story was further complicated by discontinuous follow up; emergency admissions typically being under the general physicians and ENT surgeons, and routine follow up being with the rheumatologists.

The investigation of recurrent anaemia in patients with chronic diseases such as ankylosing spondylitis is not always straight forward. Simple investigations that should be considered in addition to full blood count, red cell indices, and markers of inflammation such as erythrocyte sedimentation rate, and C reactive protein include: B12, folate, iron, total iron binding capacity, and ferritin values. These simple laboratory tests will very often distinguish the two commonest types of anaemia seen in rheumatology, iron deficiency anaemia and anaemia of chronic disease (table 1), although a bone marrow examination on occasion may be required to confirm iron stores. Although in pre-menopausal women microcytic hypochromic anaemia may often be secondary to heavy menstrual bleeding, in men, bleeding, usually from the gastrointestinal tract, should always be suspected. Investigations that might be required to identify the site of possible bleeding include upper gastrointestinal endoscopy, colonoscopy or barium enema, and small bowel follow through. Advice from a gastroenterologist may prove helpful especially when considering rarer diagnoses and further investigations such as a technetium scan for a Meckel's diverticulum, and angiography. Patients with chronic rheumatic conditions are frequently anaemic with several causes for anaemia often being present together. Falls in Hb that are not clearly related to active inflammation, which occur frequently, or that are out of proportion to the disease severity should be investigated fully and a high index of suspicion for occult bleeding is recommended. A microcytic hypochromic anaemia will very often reflect active bleeding but will only very rarely be related to anaemia of chronic disease. Investigation of this patient's small bowel may have changed the course of events and it is clear that silent or active Crohn's disease as a cause for anaemia or symptoms in patient's with ankylosing spondylitis should never be forgotten.

Active inflammatory bowel disease has been reported in as many as 4% of patients with ankylosing spondylitis,[1] in comparison with 0.05% of the population when randomly screened.[2] Ileocolonoscopy studies have shown either macroscopic or microscopic abnormalities to be present in the terminal ileum in 30–50% of patients with ankylosing spondylitis and associated peripheral arthritis.[3–5] Permeability studies using CrEDTA have also shown increased levels of intestinal permeability in patients with ankylosing spondylitis [6] and first degree relatives of patients with ankylosing spondylitis.[7] To further complicate matters NSAIDs have also been shown to increase small intestinal permeability and inflammation.[8–10]

Although terminal ileal Crohn's disease was responsible for the fatal outcome in this case, NSAID gastropathy is a well recognised phenomenon and prophylaxis against this condition, especially in patients at particular risk, such as women, those over 60 years of age, and patients with a history of previous gastrointestinal tract disease, should be considered. This was reflected in the above case both in the commencement of ranitidine when the patient first presented to the rheumatology department and in the subsequent change to misoprostol. Misoprostol has been shown to be effective long term protection against NSAID associated gastrointestinal side effects and is thought to be the preferred agent in this respect.[12]

The lesson

- The small bowel should not be overlooked as a site of bleeding in patients with rheumatic disease taking NSAIDs.
- Silent or active Crohn's disease as a cause for anaemia or symptoms should not be forgotten in patients with ankylosing spondylitis.

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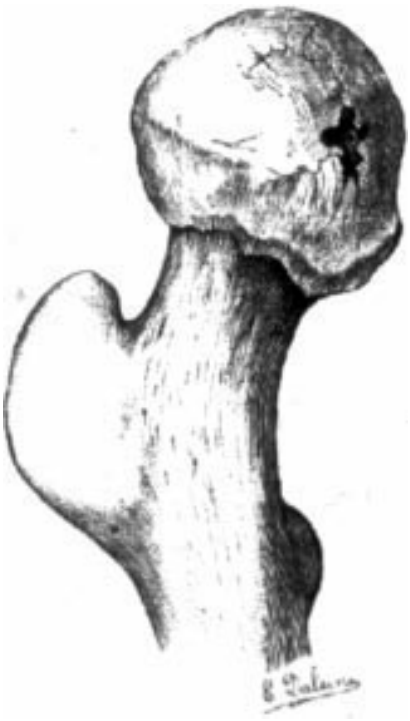

Figure 1 Tuberculous arthritis of the hip. Deep cavity on the femoral head.

Comment

The observation of these lesions at the end of the 19th century suggested that infection of the hip joint originated from a focus in the subchondral bone.

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